



# **Armed Forces College of Medicine AFCM**





# **Demyelinating Diseases**

**By**  
**Dr Noha El Anwar**





# Good Morning

*Have a Nice Day*



# INTENDED LEARNING OBJECTIVES (ILO)



**By the end of this lesson the student will be able to:**

1. Discuss demyelinating diseases
- 2. Describe pathological changes of multiple sclerosis**
3. Analyse given data to diagnose pathological conditions of Demyelinating diseases based on given clinical, radiologic data and/or laboratory findings



# Demyelinating Diseases



❖ **Within the CNS**, axons are tightly ensheathed by **myelin**, an electrical insulator that allows rapid propagation of neural impulses.

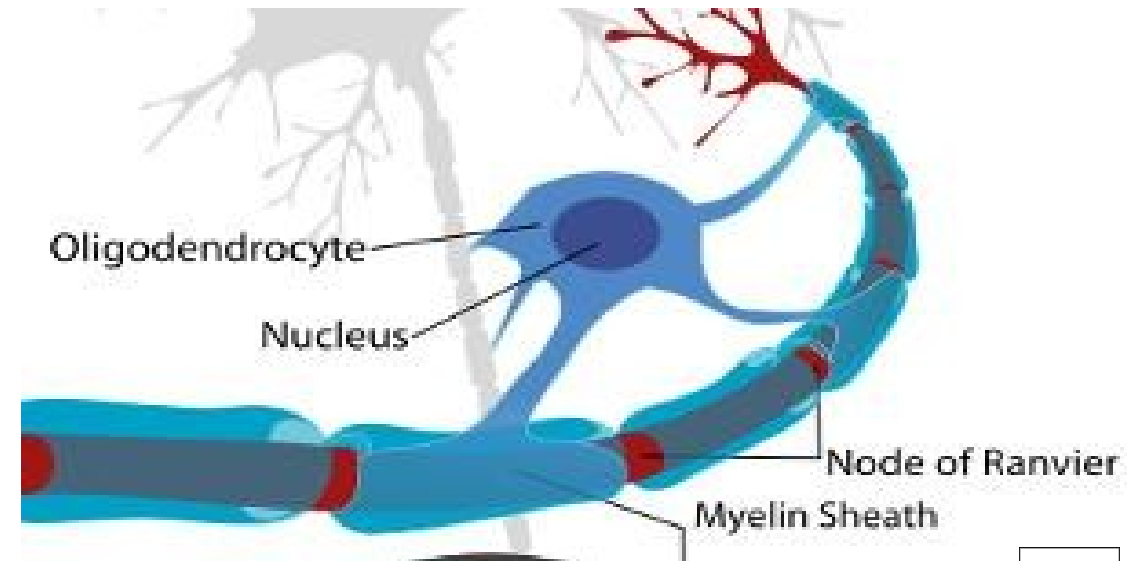
❖ **Myelin** is assembled by **oligodendrocytes**.

❖ Although myelinated axons are present in all areas of the brain, they are the dominant component in **the white matter**; therefore, most diseases of myelin are **primarily white matter disorders**.

## WHAT IS MYELIN SHEATH?

**Myelin sheath is a white electrically insulating sheath that surrounds the axon of nerve cells. Myelin sheath protects and insulates the axon.**

<http://www.quizcrazy.in/icse-class-10-biology/nervous-system-flashcards/nervous-system-notes-define-myelin-sheath.png>



<https://s3.amazonaws.com/classconnection/336/flashcards/10618336/myelin-152DE15D95A1630C5CA.jpg>



# Demyelinating Diseases



**CNS diseases involving myelin are separated into two broad groups:**

**A) Acquired conditions** characterized by damage to previously normal myelin.

- 1- The most common diseases in this group result from immune-mediated injury, such as **multiple sclerosis** (MS)
- 2- **Viral infection** of oligodendrocytes.
- 3- **Injury caused by drugs** and other toxic agents.



# Demyelinating Diseases



## B) Inherited demyelinating diseases (Leukodystrophies) :

- Caused by **abnormal myelin synthesis or turnover**.
- Most of these are caused by **mutations** that disrupt the function of proteins required for the formation of normal myelin sheaths.
- Most are of **autosomal recessive inheritance**.
- There is typically **diffuse involvement of white matter** leading to deterioration in motor skills, spasticity, hypotonia, or ataxia.





# Multiple Sclerosis



- **Multiple Sclerosis** is a chronic relapsing-remitting disorder of probable **autoimmune origin** characterized by **recurrent episodes** of demyelination in the brain(including optic nerves) and spinal cord.
- it results in progressive **neurological deficits**.
- **Women** have 2x the risk of men.
- **Genetic and environmental factors contribute to the pathogenesis:**

1- **HLA DR 15** confers genetic susceptibility.



# Multiple Sclerosis



- **Pathogenesis :**

**The lesions of MS are caused by an autoimmune response directed against components of the myelin sheath.**

- The disease is initiated by **T cells** that react against myelin antigens and **activate macrophages**, promote the recruitment of leukocytes.
- The demyelination is caused by **activated leukocytes and their injurious products.**
- **The infiltrate in MS plaques** and surrounding regions of the brain consists **mainly of T cells and macrophages.**



# Multiple Sclerosis



- **MS is primarily a multifocal white matter disease.**
- Characteristic lesions, termed **plaques**.

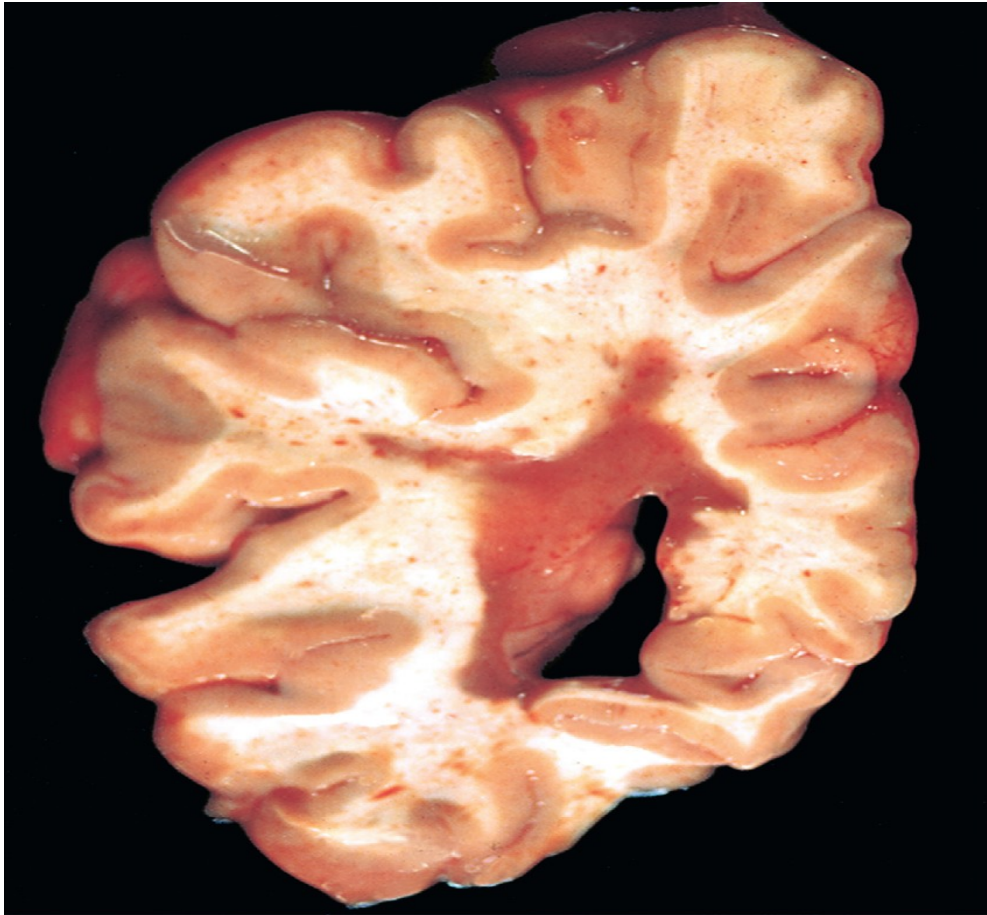
## **On gross examination :**

- Show well-circumscribed **gray lesions (plaques)**.
- **Bilateral** in distribution
- **Usually Periventricular**.



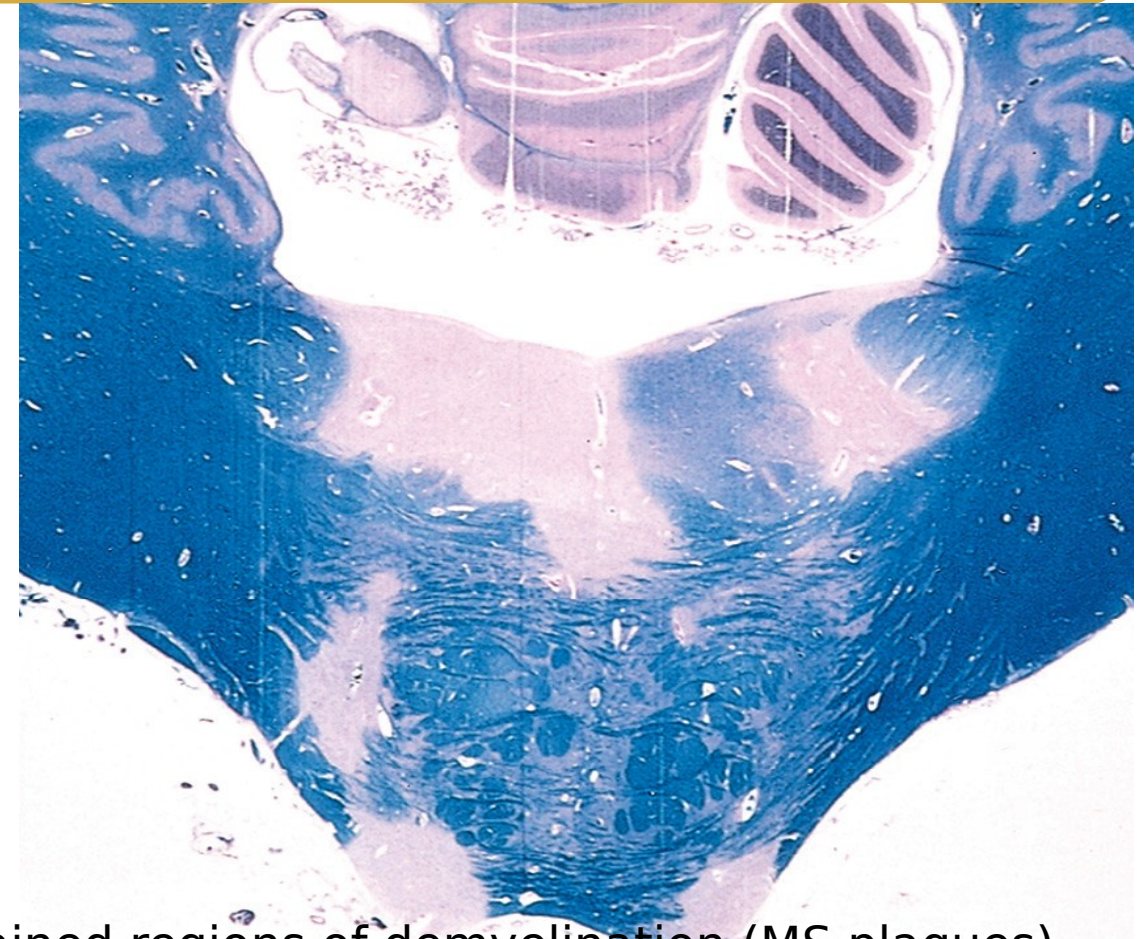


# Multiple Sclerosis



Section of fresh brain showing a plaque around the lateral ventricle.

Robbins basic pathology, 10<sup>th</sup> edition, 2018



Unstained regions of demyelination (MS plaques) around the fourth ventricle. Luxol fast blue-periodic acid-Schiff stain for myelin.

Robbins basic pathology, 10<sup>th</sup> edition, 2018



## Microscopic Examination:

### Active plaques:

- Contain abundant **macrophages** stuffed with **myelin debris**.
- **Lymphocytes** are present, mostly **perivascular**.

### Inactive plaques:

When plaques become quiescent, the **inflammation mostly disappears** leaving **little to no myelin**, astrocytic proliferation and **gliosis**.

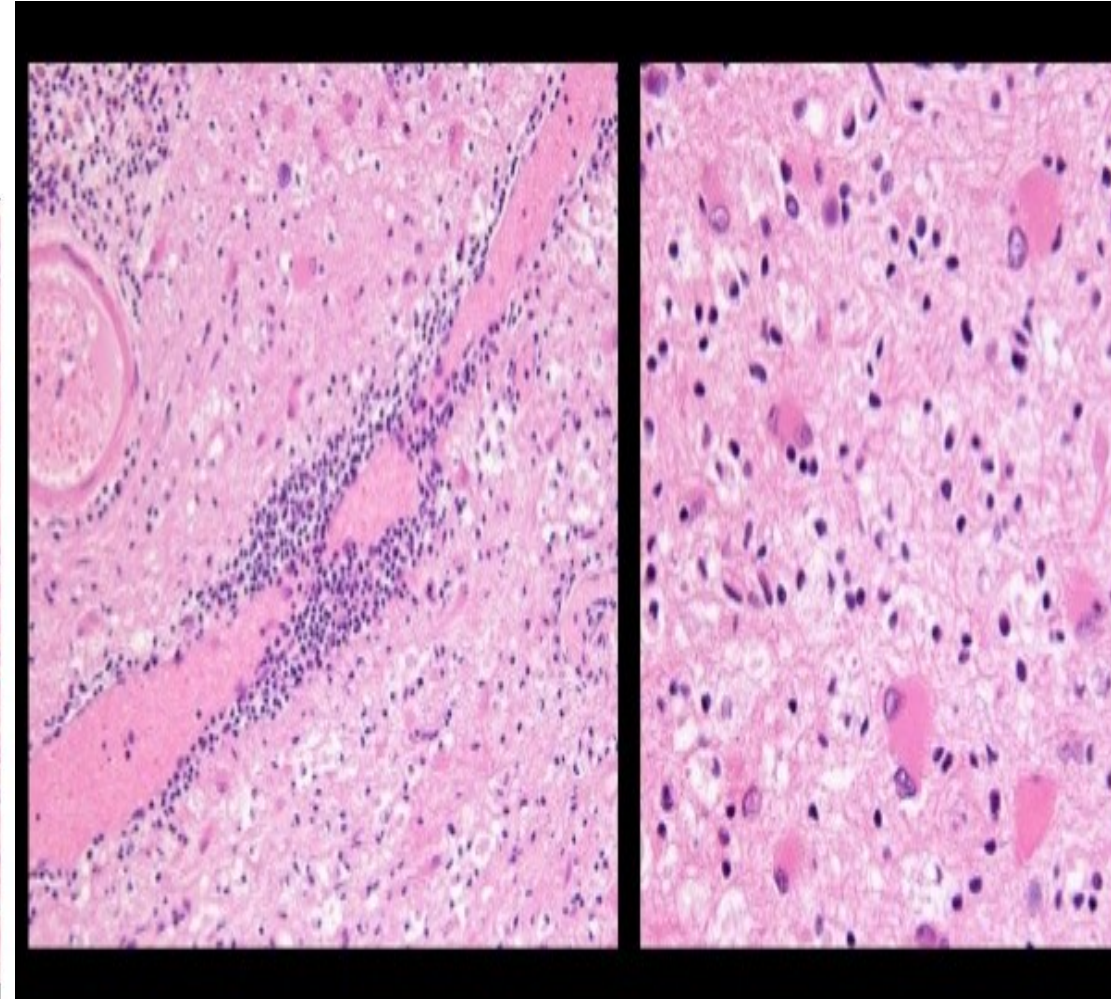
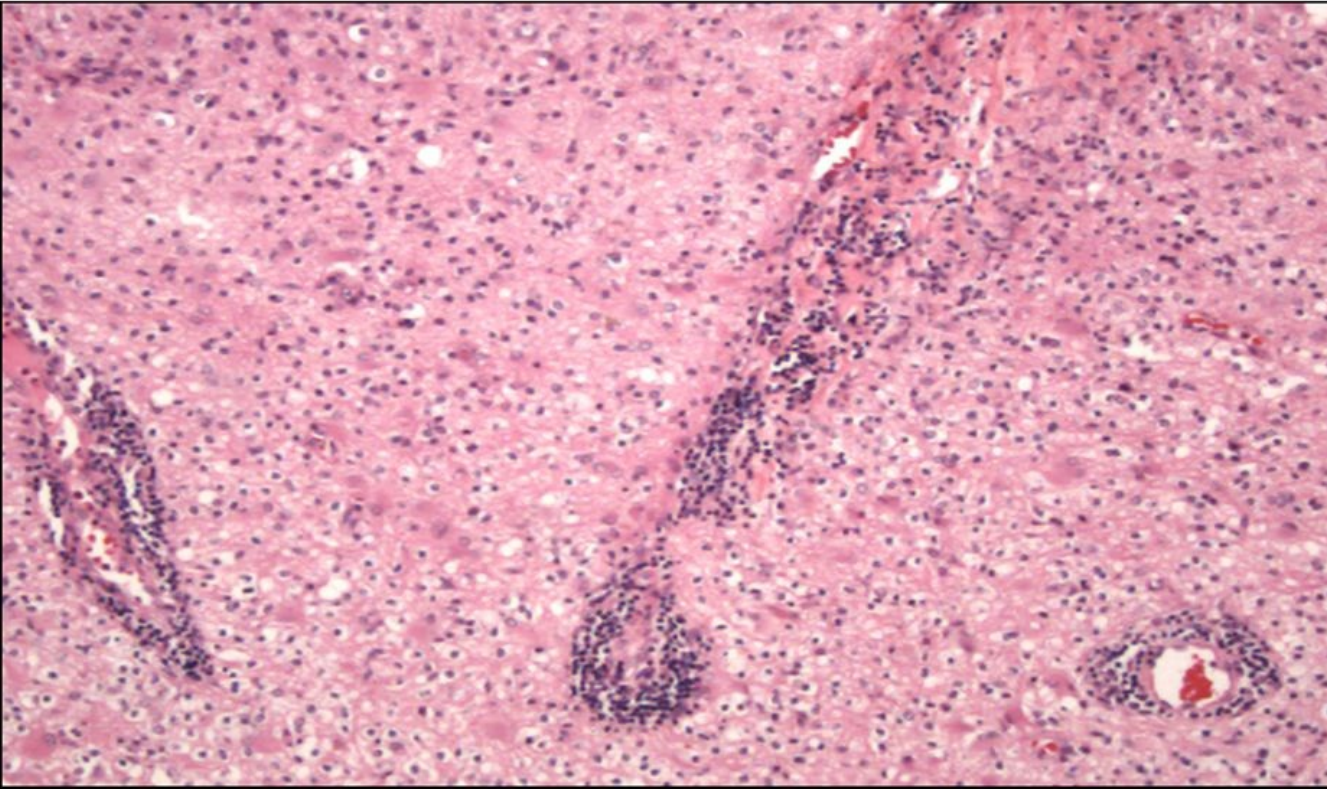




# Multiple Sclerosis



**Multiple sclerosis, active plaque, microscopic:** Active plaques contain perivascular lymphocytes, mostly T cells, macrophages and reactive astrocytes.



<https://image.slidesharecdn.com/npresidentlecture-wmdisease2009-slideshareupload-111117145302-phpapp01/95/npresident-lecturewmdisease2009slideshareupload-42-728.jpg?cb=1321543881>



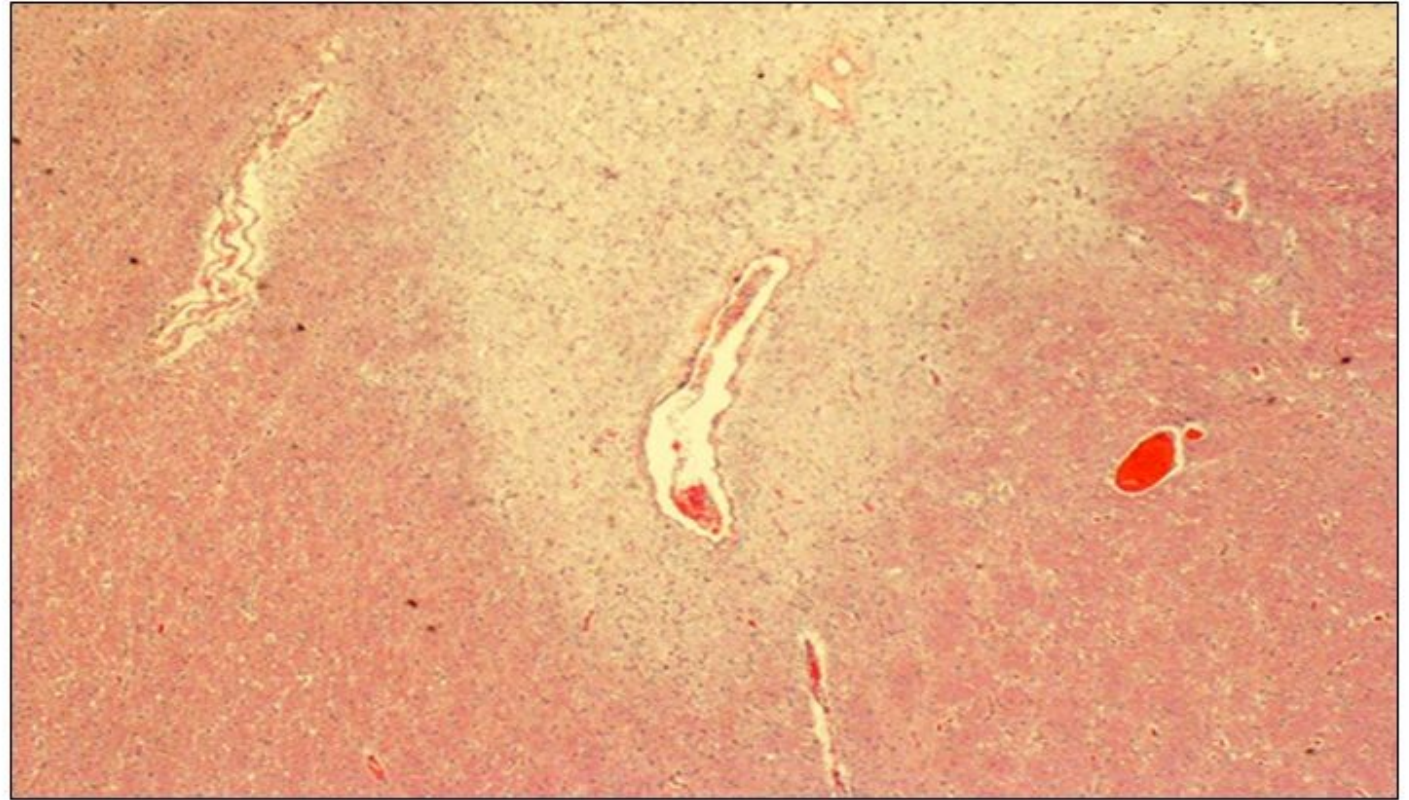


# Multiple Sclerosis



## Inactive plaques:

The **inflammation mostly disappears** leaving **little to no myelin, astrocytic proliferation and gliosis.**



*This is an H&E stained sections from a patient with long-standing MS. This lesion is centered on a vein. In this older lesion, however, there is very little inflammation around the vein. You can see the loss of myelin even without a special stain: it is lighter pink than the normal white matter surrounding it.*

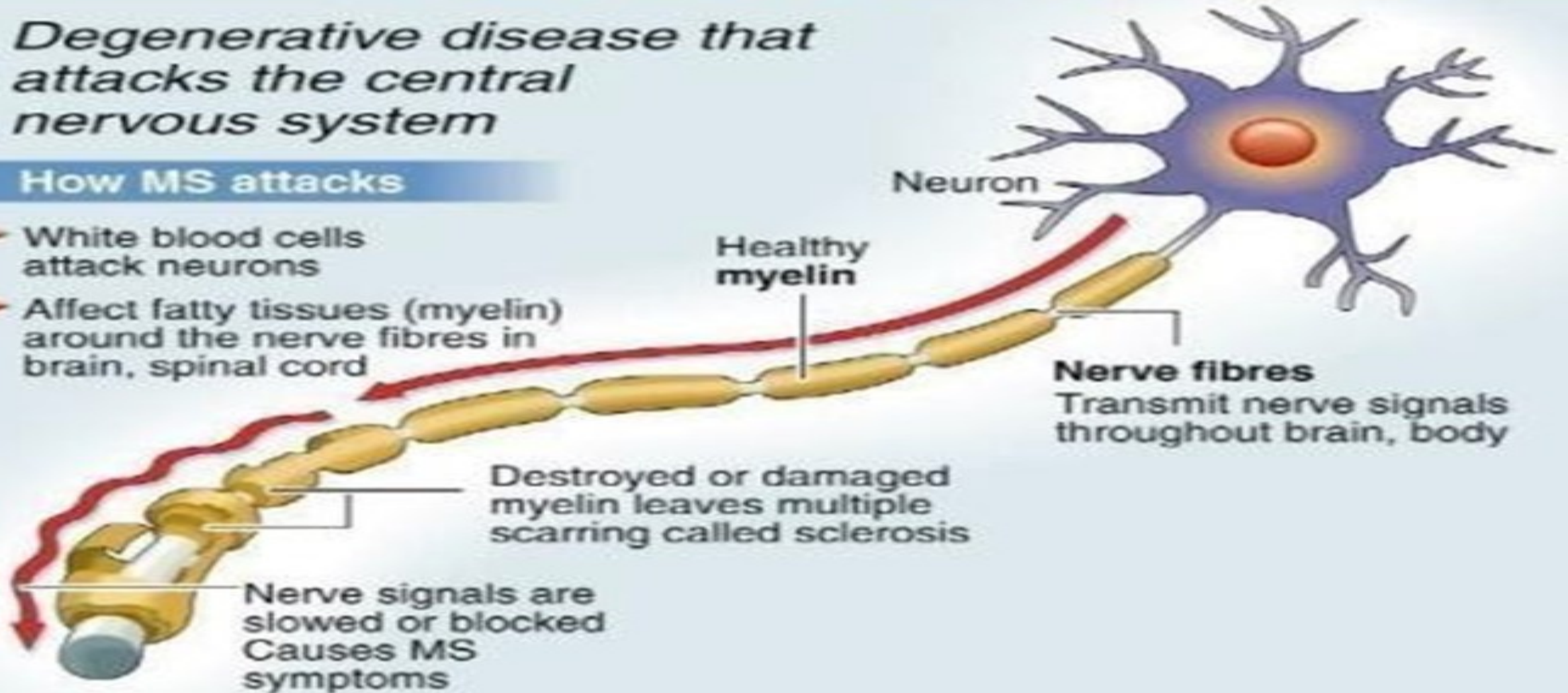


# Multiple sclerosis

*Degenerative disease that attacks the central nervous system*

## How MS attacks

- ▶ White blood cells attack neurons
- ▶ Affect fatty tissues (myelin) around the nerve fibres in brain, spinal cord



Sources: Harvard/NMSA/MayoClinic

AFP

[http://2.bp.blogspot.com/\\_NFwUaRgXjpk/S162kdpAk9I/AAAAAAAAAAM/OYZ-WEft0J4/w1200-h630-p-k-no-nu/MS.jpg](http://2.bp.blogspot.com/_NFwUaRgXjpk/S162kdpAk9I/AAAAAAAAAAM/OYZ-WEft0J4/w1200-h630-p-k-no-nu/MS.jpg)





## Clinical onset:

- It is typically in **decades 3-4**.
- About 85% of cases show a **relapsing remitting course**.  
Recovery from each episode of demyelination occurs in weeks or months.
- **During an acute attack**, nerve conduction is entirely blocked, leading to **acute neurological deficits**.
- **Chronic plaques** are associated with **slower nerve conduction, allowing for partial recovery**.



# Multiple Sclerosis



- **Recurrent attacks** cause **progressive neurological deterioration**.
- **Early symptoms** include **sensory problems, paresis, and visual dysfunction**.
- **As the disease progresses**, other symptoms include fatigue, bladder dysfunction, spasticity and ataxia.





# Central pontine myelinolysis (CPM)



- It is caused by **nonimmune damage to oligodendrocytes** typically after sudden correction of **hyponatremia**.
- The condition is very often fatal.
- Patients at risk include the severely malnourished and alcoholics with liver disease.







# **CNS module**

## **Practical lesson**

### **Diseases of CNS**



# INTENDED LEARNING OBJECTIVES (ILO)



**By the end of this lesson the student will be able to:**

- 1- Describe the gross picture of Meningioma, Cerebellar astrocytoma and Cerebral haemorrhage.
- 2- Describe the microscopic picture of Meningioma, schwannoma and Glioblastoma Multiforme.
- 3-Analyze the findings of the clinical case.
- 4-Correlate between clinical data and histopathological data  
to reach a final diagnosis



# CNS Gross Specimens



- ☐ **Meningioma**
- ☐ **Cerebellar astrocytoma**
- ☐ **Cerebral hemorrhage**



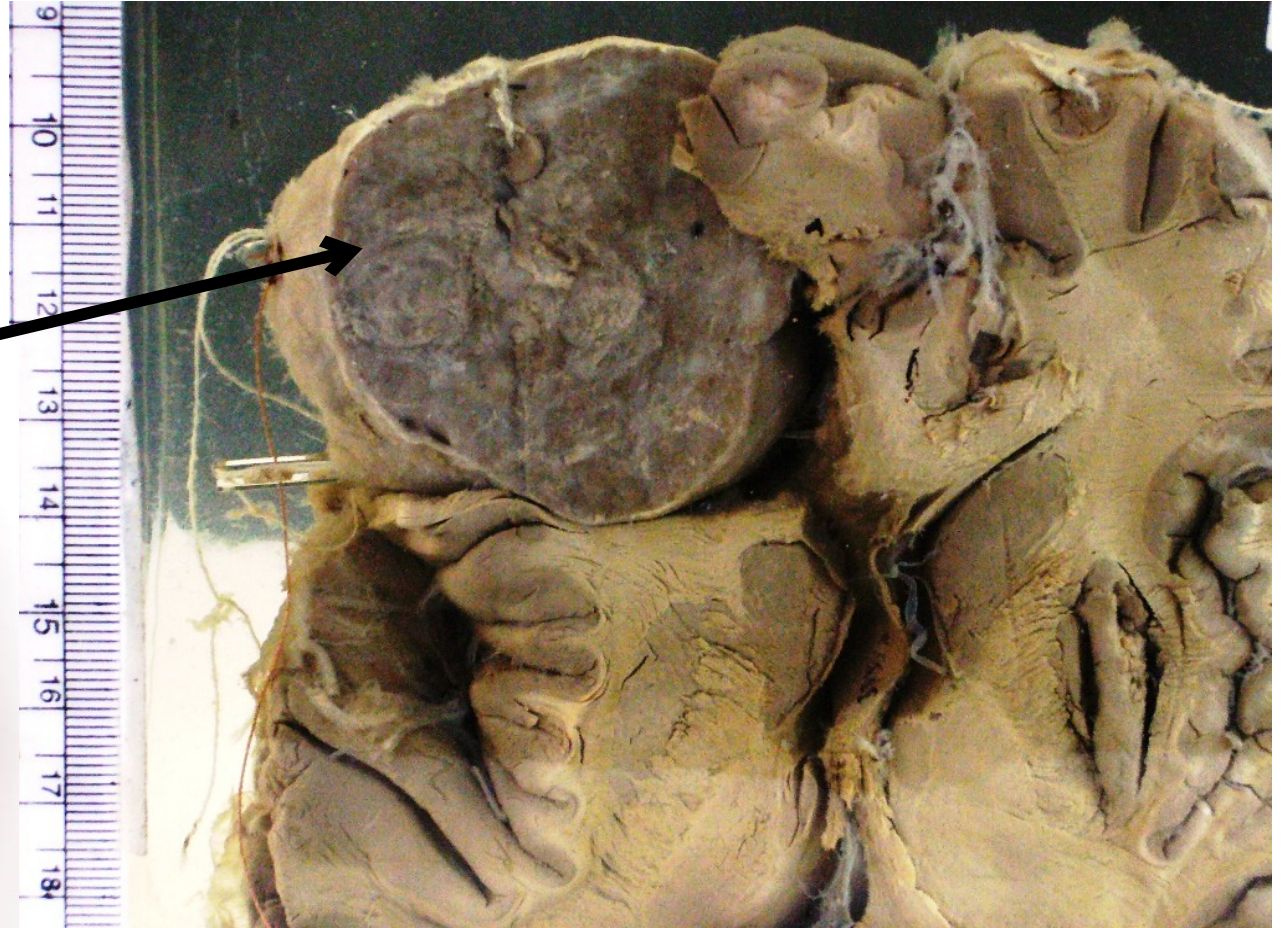
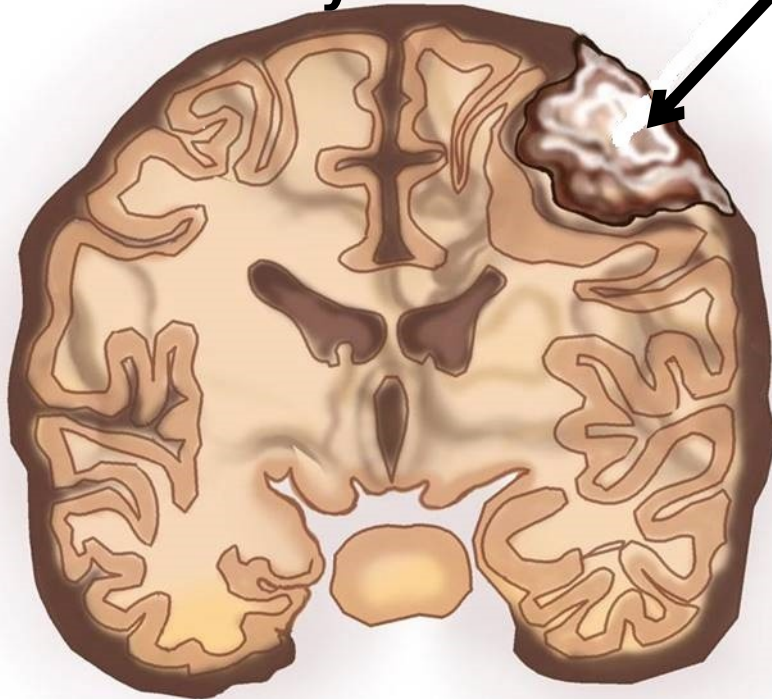
# MENINGIOMA



## Describe

Lesion  
Site  
Size  
Shape  
Colour  
Cut section

**Capsulated single mass**  
**In frontal lobe**  
**Rounded .....x.....**  
**Greyish white**  
**Whorly cutsection**





# MENINGIOMA



Capsulated mass

## Specimen:

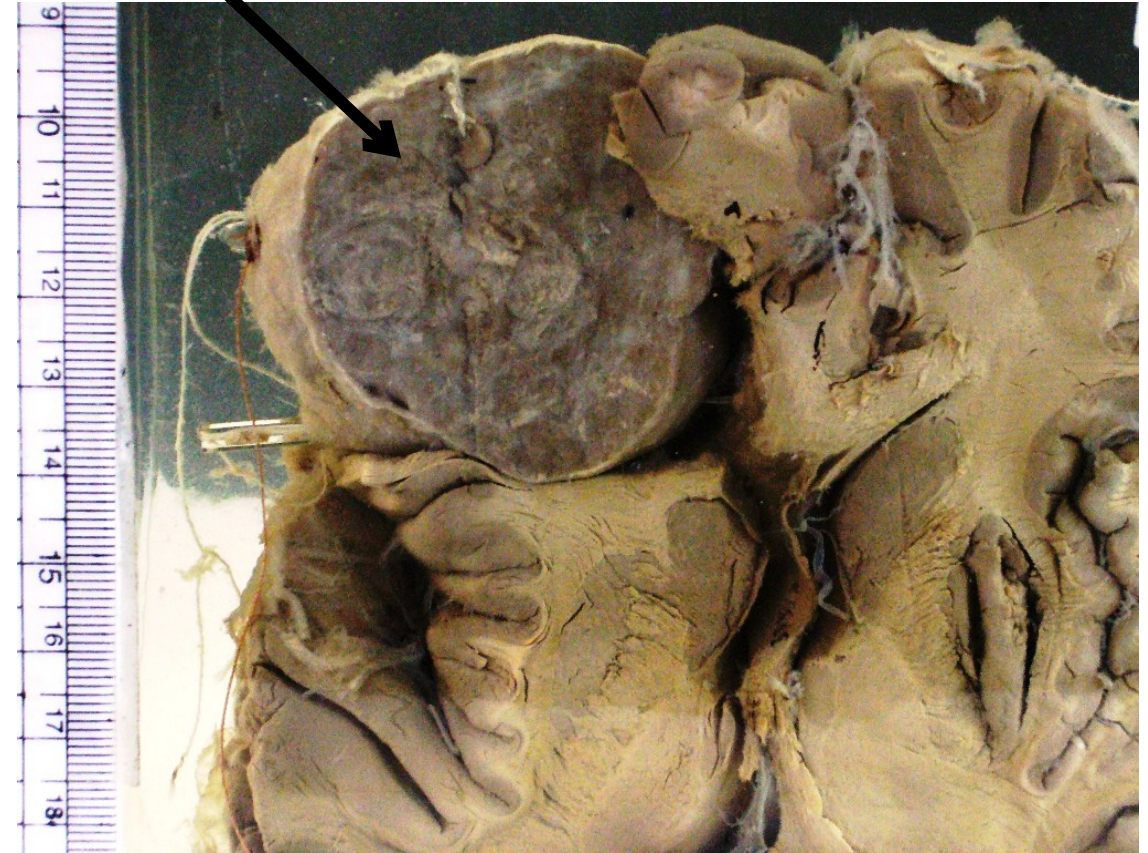
**Transverse section of the brain.**

## Comment :

1. An encapsulated rounded mass
2. Compressing but not infiltrating anterior part of frontal lobe.
3. Cut section of the mass is greyish white in colour and shows whorly appearance

## Diagnosis:

**Meningioma**



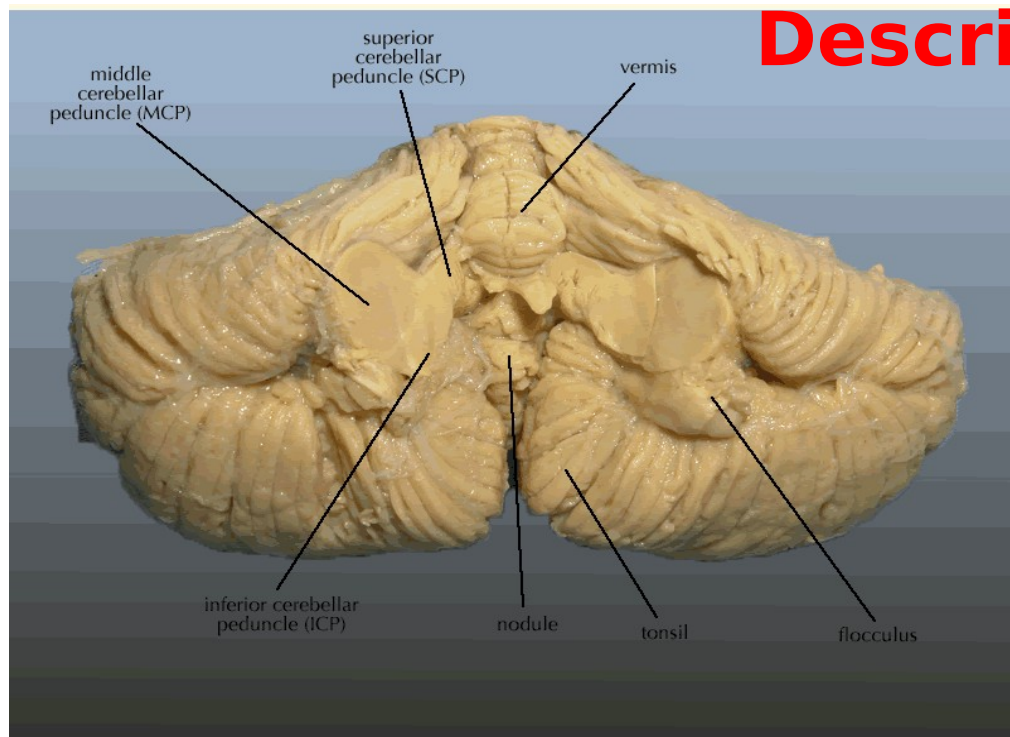
Atlas of Museum Jaers, Pathology Department ,Ain Shams University



# Cerebellar Astrocytoma



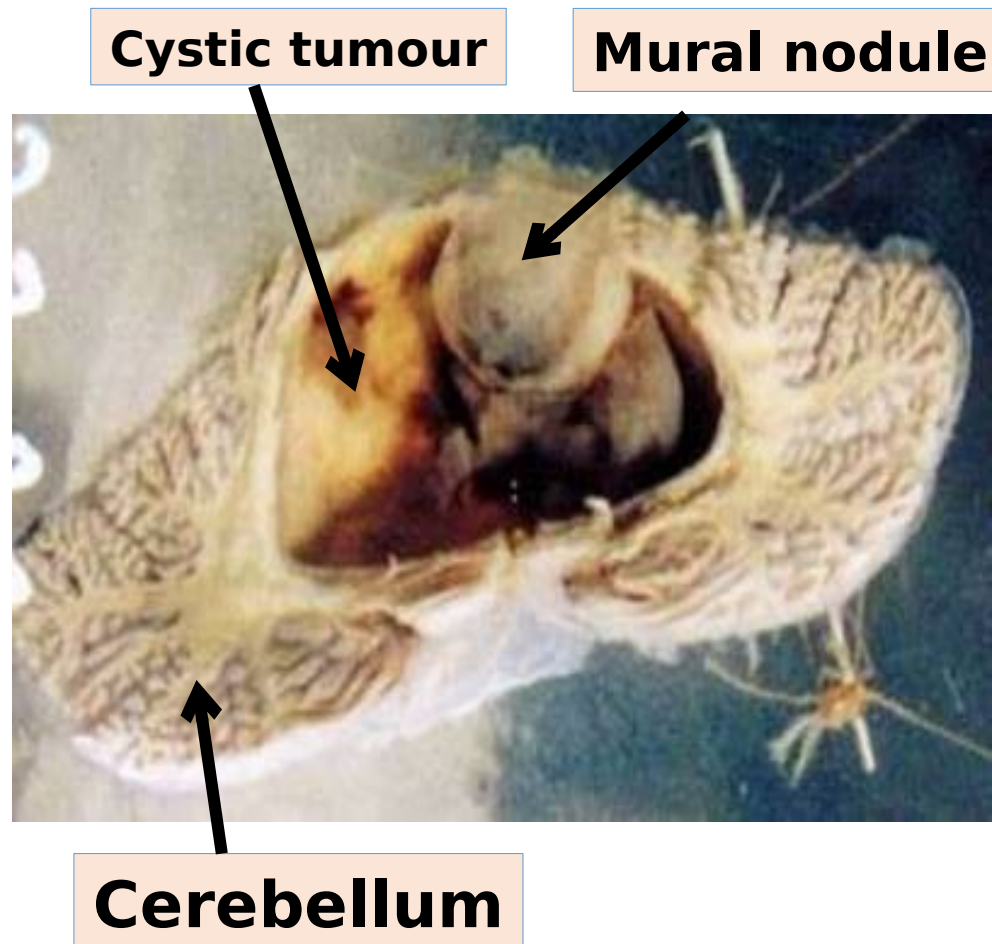
## Compare & Describe



**Normal cerebellum**

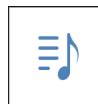
<http://slideplayer.com/8423519/26/images/11/Anterior+view+What+do+the+nodulus+and+flocculus+do+Vestibulocerebellum+%E2%80%93+balance+in+gait+and+stance+%2C+integration+of+eye+movements..jpg>

9/20/24



**Cerebellum**

Pathology department, Cairo university



# Cerebellar Astrocytoma



## Specimen:

Section in the cerebellum.

## Comment:

1. Cut section shows a cystic tumour
2. Upper part of cyst shows a white nodule projecting inside the cyst cavity (mural nodule).

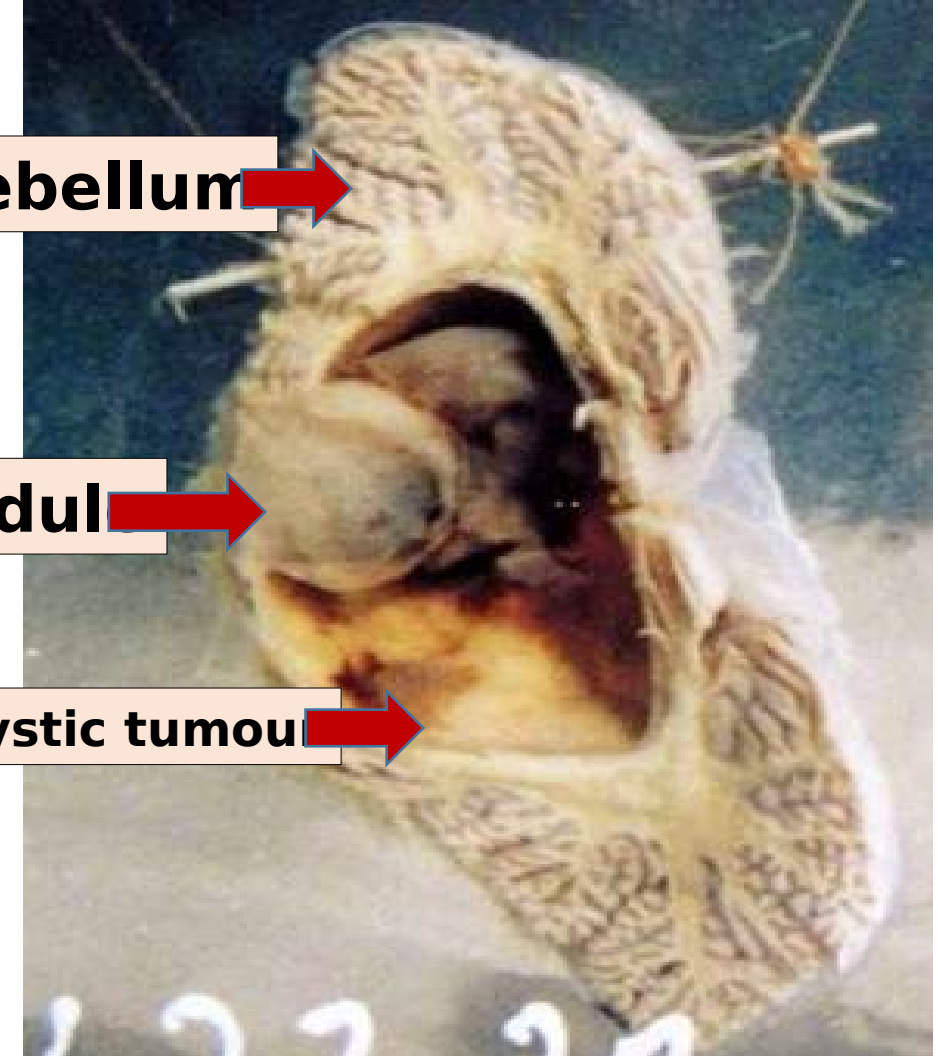
## Diagnosis:

**Cerebellar astrocytoma.**

Cerebellum →

mural nodule →

Cystic tumour →





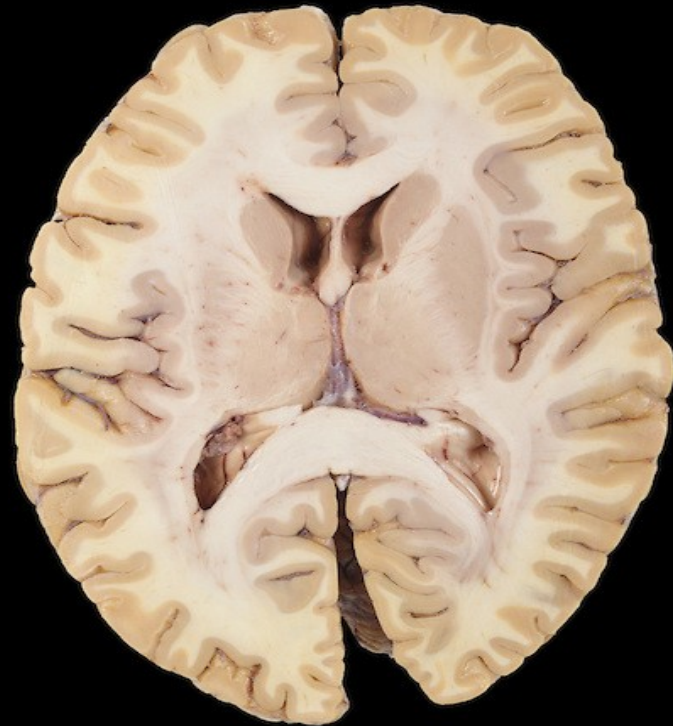
# Cerebral Hemorrhage



Section in normal brain

**Compare &  
Describe**

Lateral ventricles  
with brown clotted  
blood



visuals:unlimited

[https://tse1.mm.bing.net/th?id=OIP.BO\\_t\\_9Xr4h70H4rhNHQxzAHaE9&pid=Api&P=0&w=261&h=176](https://tse1.mm.bing.net/th?id=OIP.BO_t_9Xr4h70H4rhNHQxzAHaE9&pid=Api&P=0&w=261&h=176)  
9/20/24

CNS Module

[https://i.ytimg.com/vi/B3mttcq2\\_k/maxresdefault.jpg](https://i.ytimg.com/vi/B3mttcq2_k/maxresdefault.jpg)

Basal ganglia  
with hematoma





# Cerebral Hemorrhage



## Specimen:

**Section in the brain.**

## Comment :

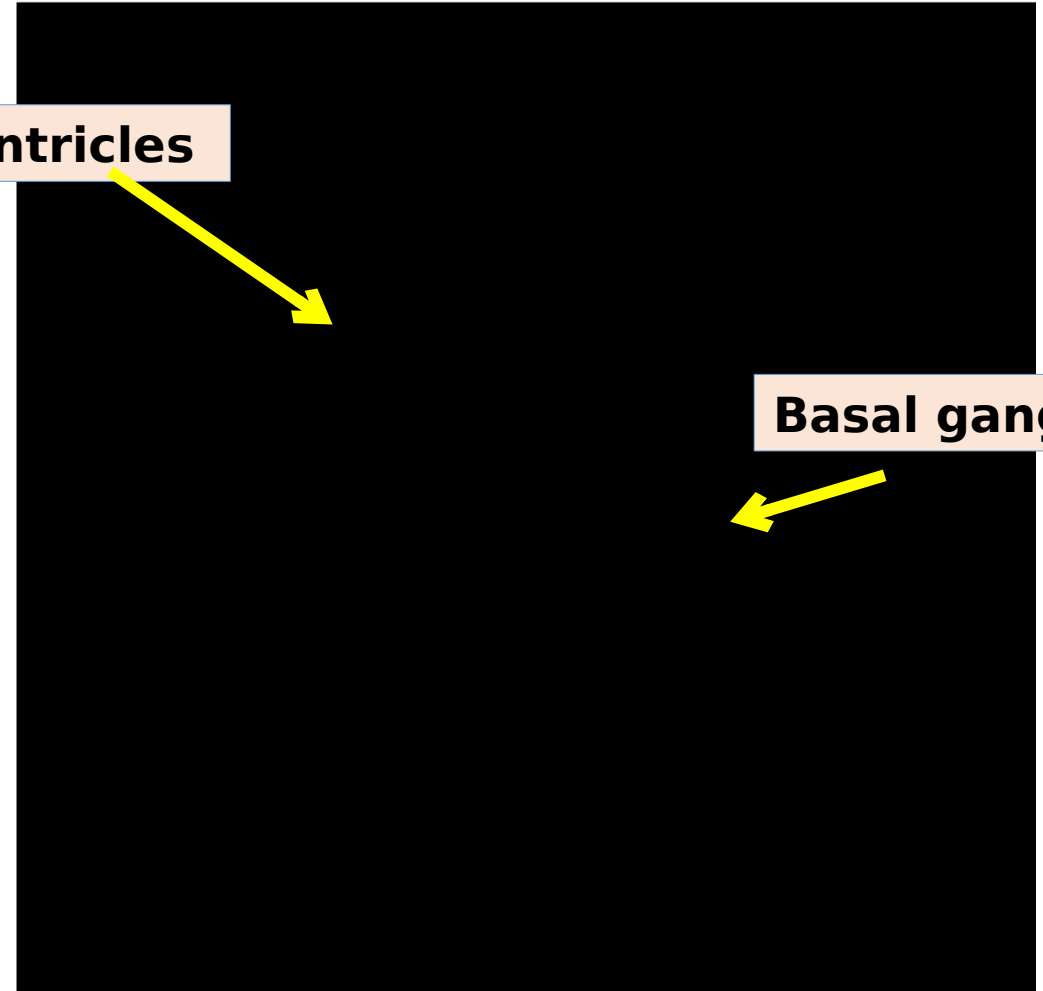
1. Right basal ganglia is destroyed and replaced by large hematoma
2. Lateral ventricles are filled with brown clotted blood .

## Diagnosis:

**Cerebral hemorrhage**

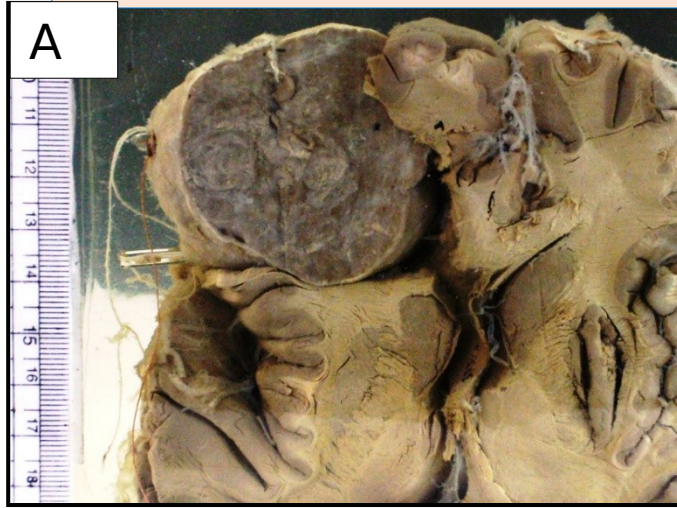
Lateral ventricles

Basal ganglia





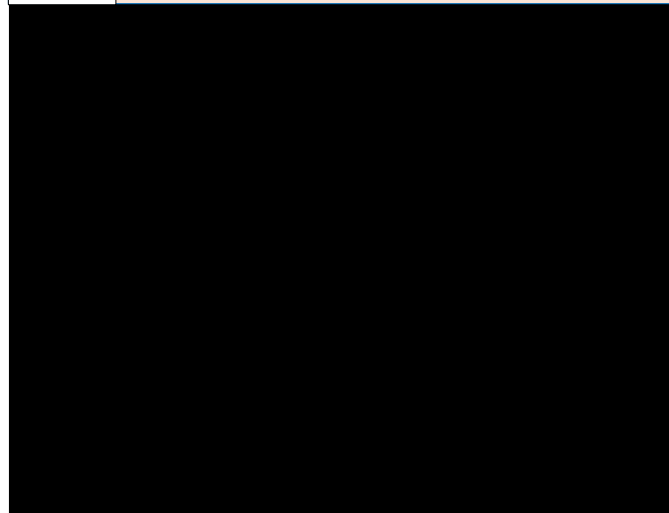
## Meningioma



## Cerebellar astrocytoma



## Cerebral hemorrhage





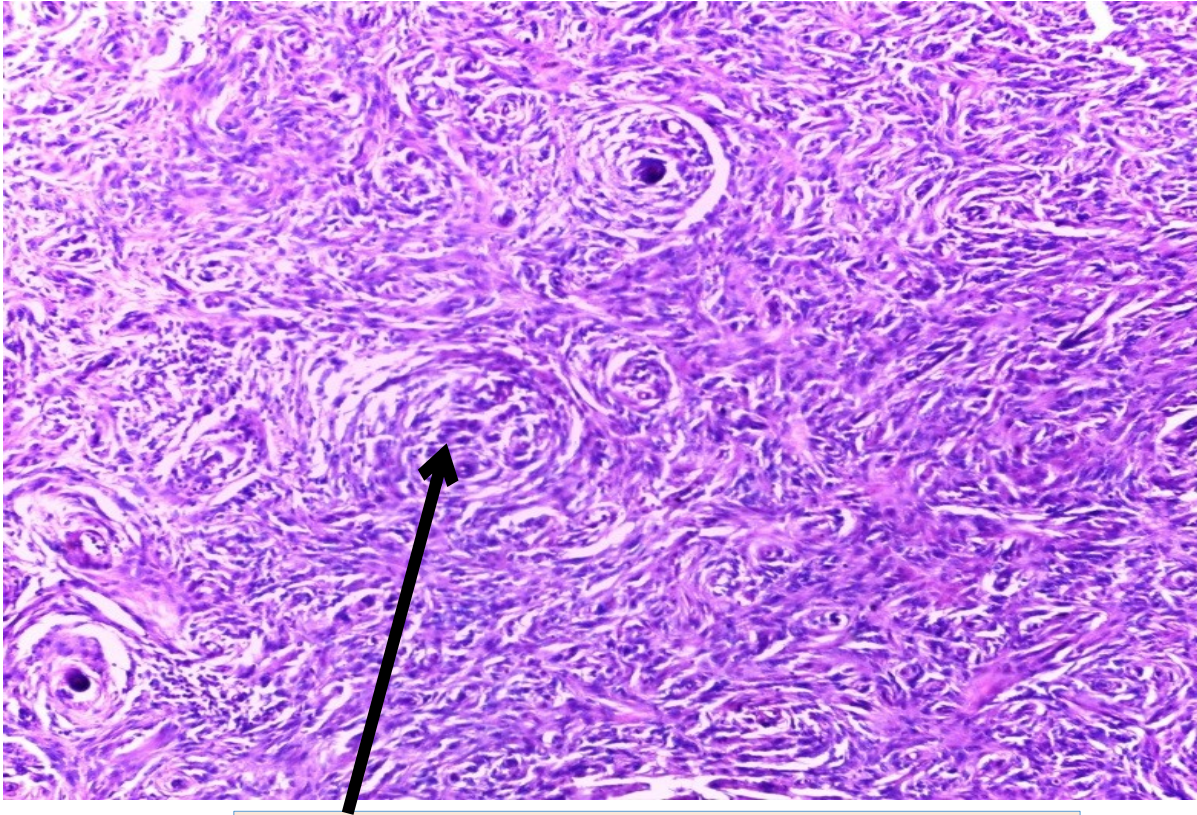
- ☐ **Meningioma**
- ☐ **Schwannoma**
- ☐ **Glioblastoma  
Multiforme**



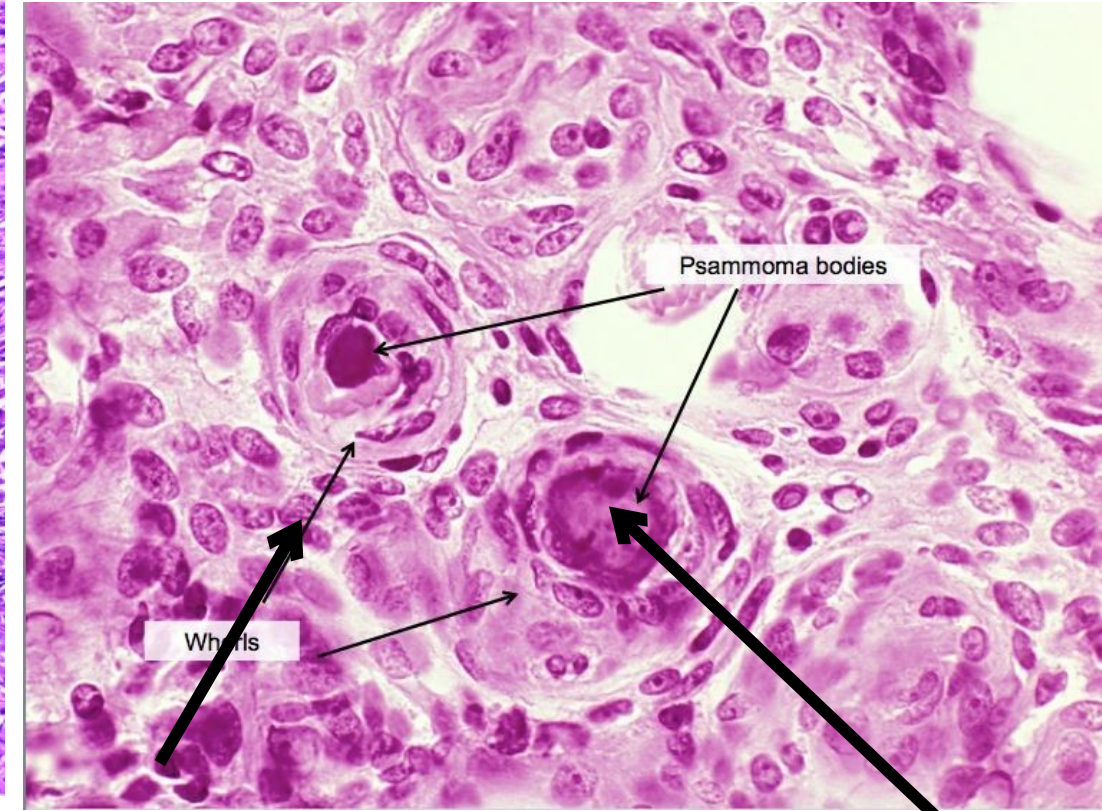


# Meningioma

## Describe



**Tumour cells in concentric whorls**



**Oval tumor cells with indistinct cell border pale cytoplasm and**

**Psammoma bodies**  
**Concentrically laminated**  
**calcified**  
**bodies dark bluish in colour**

<http://www.mrcophth.com/pathology/opticnervepathology/meningiotheliomatous.jpg>





# Meningioma



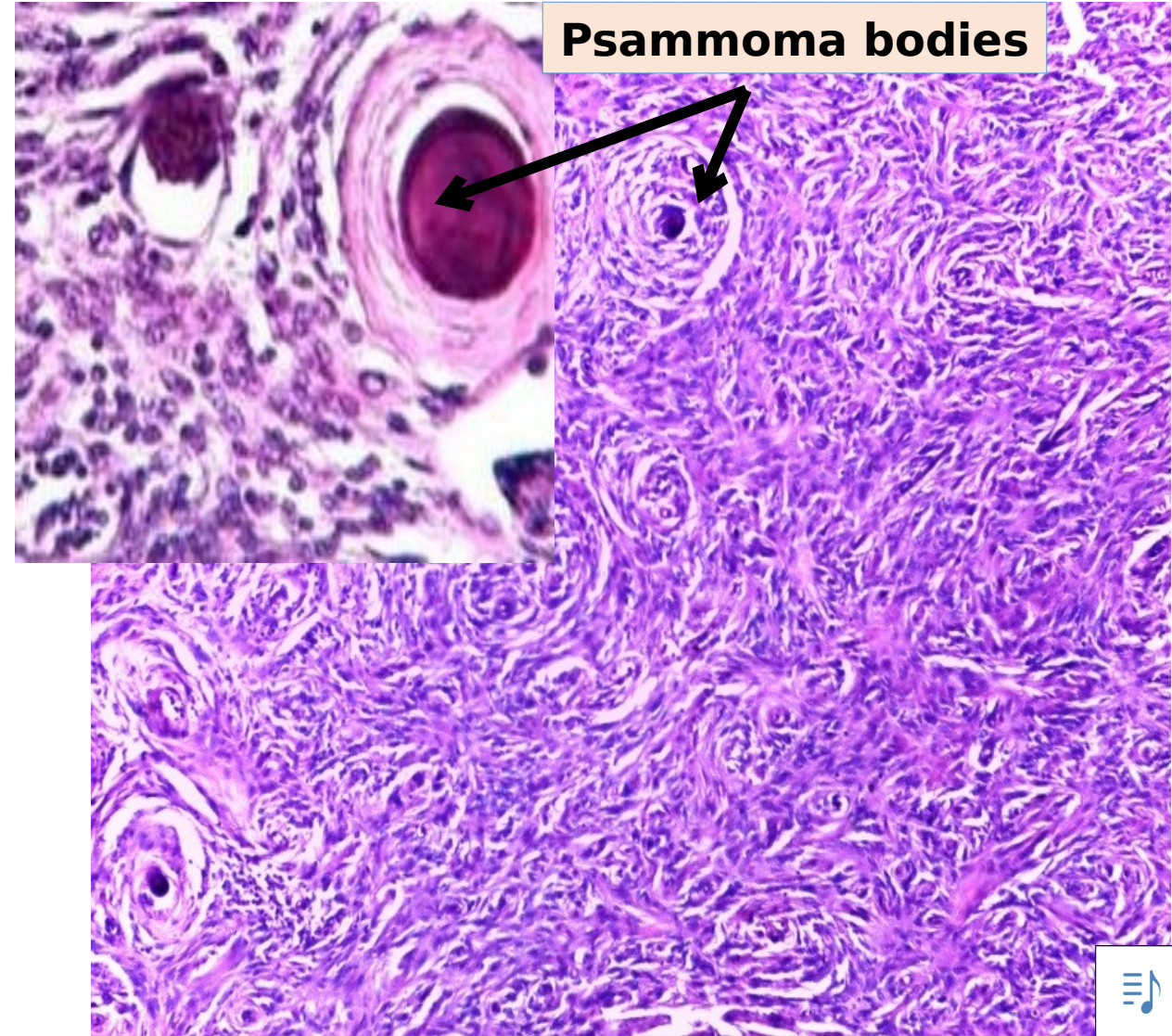
## Specimen

Section in a benign tumor originating from meningiothelial cells

## Comment

1. Tumor cells are arranged in a whorly pattern.
2. Central cells of some whorls undergo calcification and appear dark blue (**psammoma bodies**).
3. Tumor cells are oval with indistinct cell borders, pale cytoplasm and round nuclei.

**Diagnosis:** Meningioma

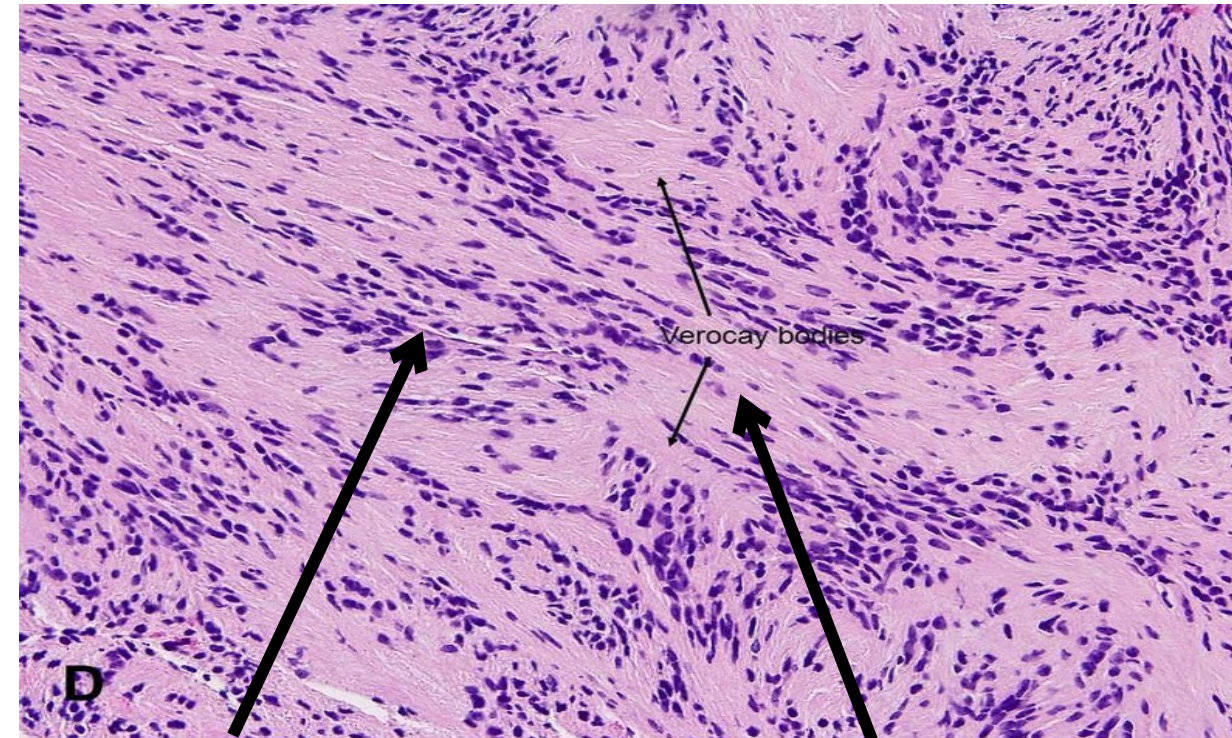
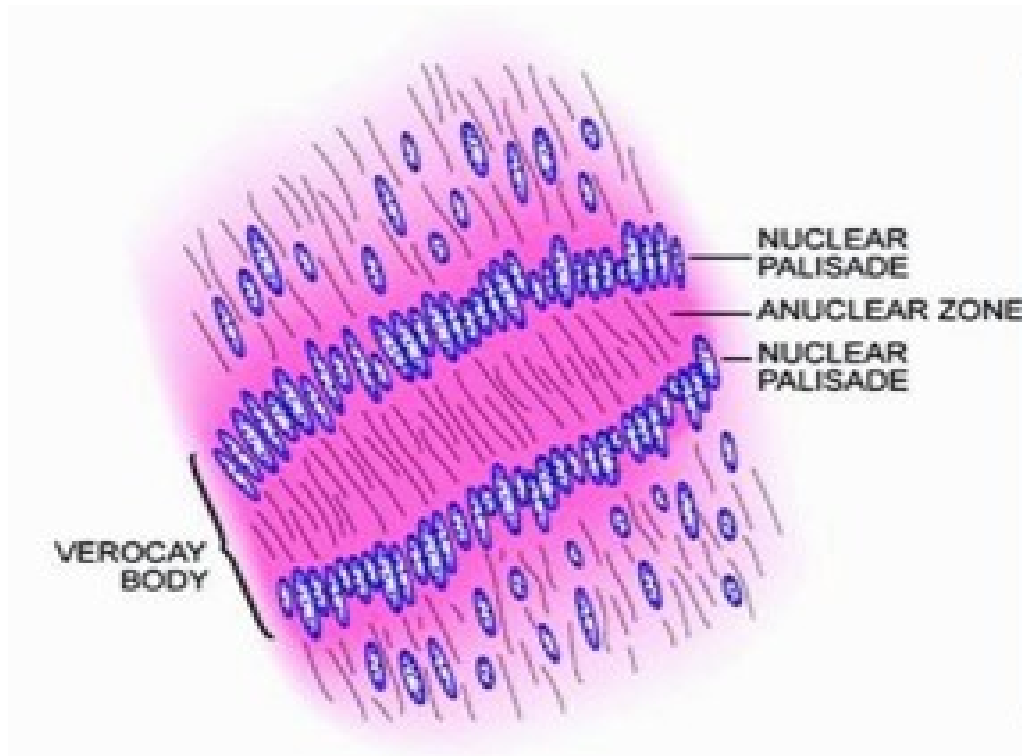




# Schwannoma



## Describe



[https://classconnection.s3.amazonaws.com/771/flashcards/1361771/png/schwannoma\\_histology1359228005842.png](https://classconnection.s3.amazonaws.com/771/flashcards/1361771/png/schwannoma_histology1359228005842.png)

- formed of elongated cells
- arranged in bundles with
- nuclear **palisading** (the nuclei are

Verocay bodies  
the cytoplasmic nuclear free zones are called "**verocay bodies**"

[http://www.auanet.org/  
images/education/  
pathology/  
retroperitoneum/  
schwannoma-](http://www.auanet.org/images/education/pathology/retroperitoneum/schwannoma-)





# Schwannoma

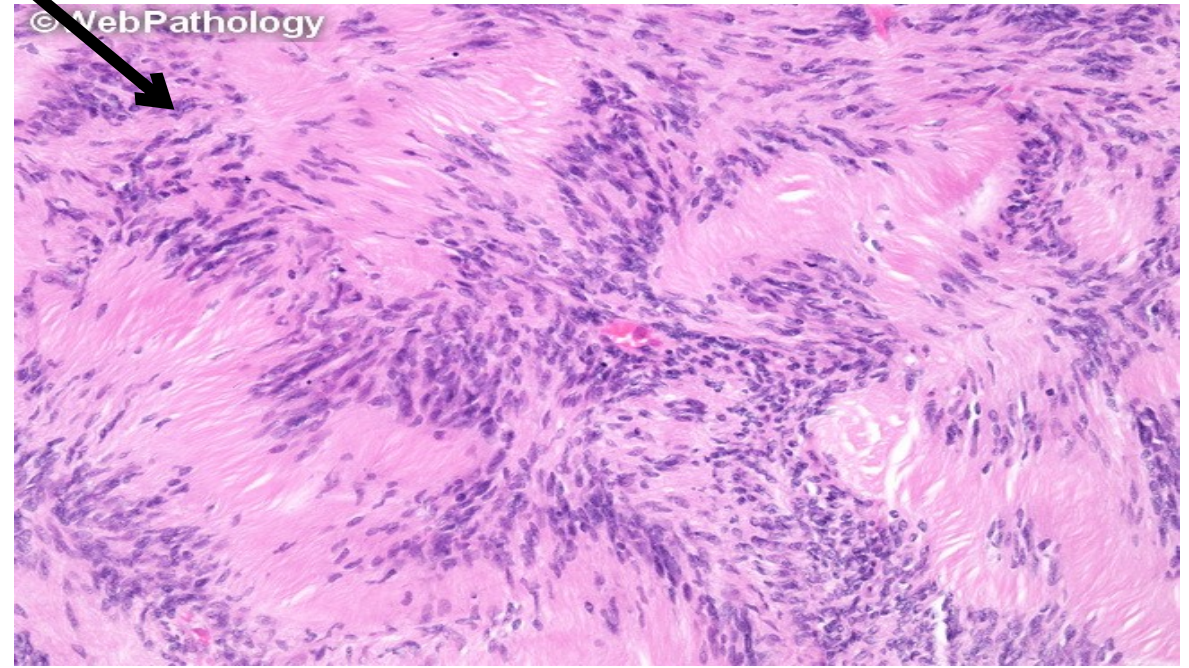
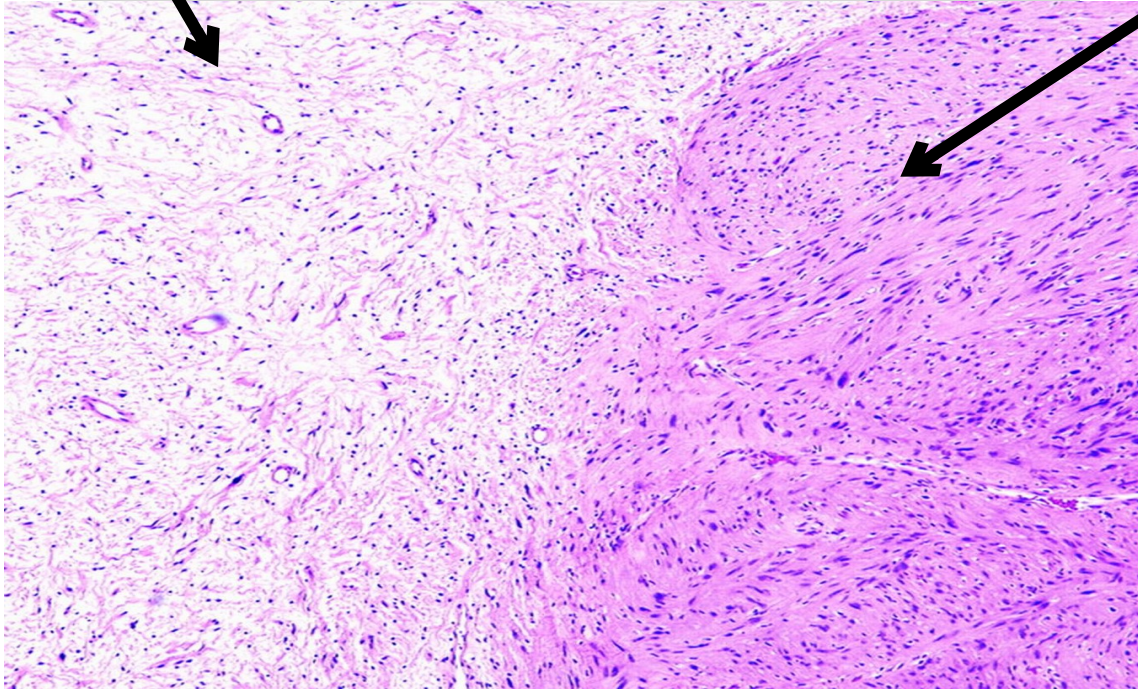


## Antoni B growth pattern:

Formed of less densely cellular elements arranged haphazardly.

## Antoni A growth pattern

- formed of elongated cells arranged in bundles with
- nuclear **palisading**
- **Verroca bodies**



<https://upload.orthobullets.com/topic/8053/images/antoni.jpg>

[https://www.webpathology.com/slides-13/slides/Schwannoma\\_AntoniA\\_VerocayBodies2.jpg](https://www.webpathology.com/slides-13/slides/Schwannoma_AntoniA_VerocayBodies2.jpg)



# Schwannoma

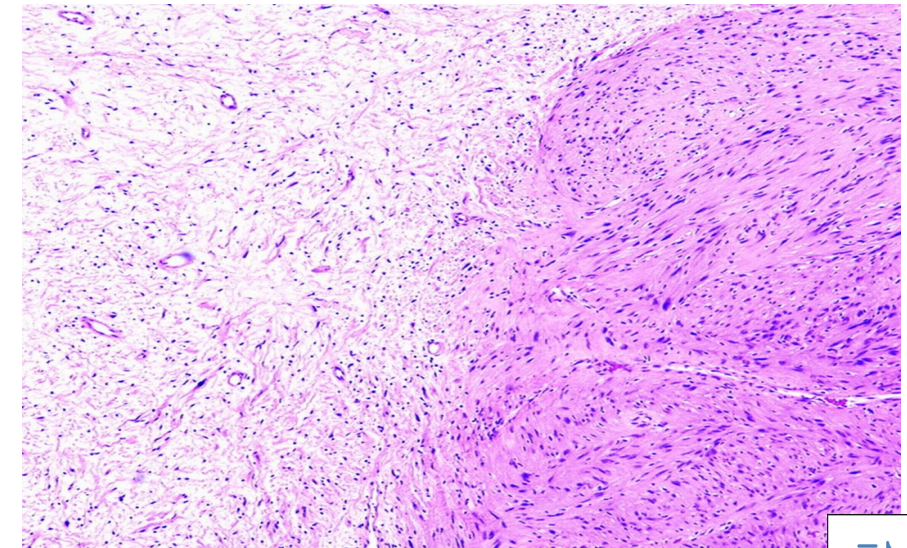
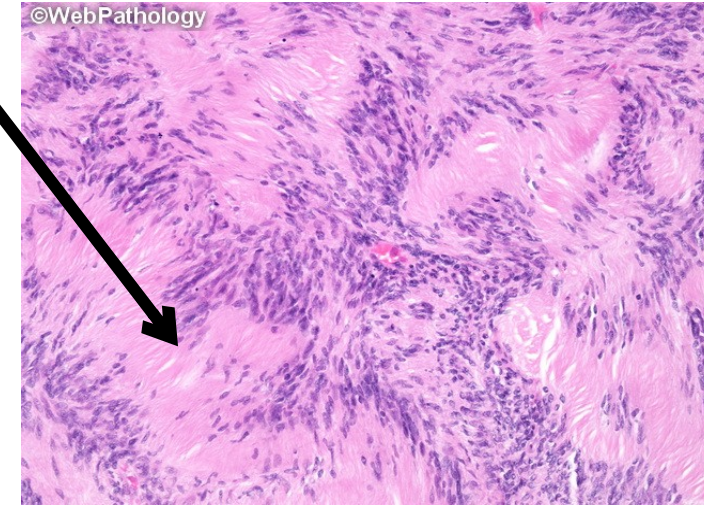
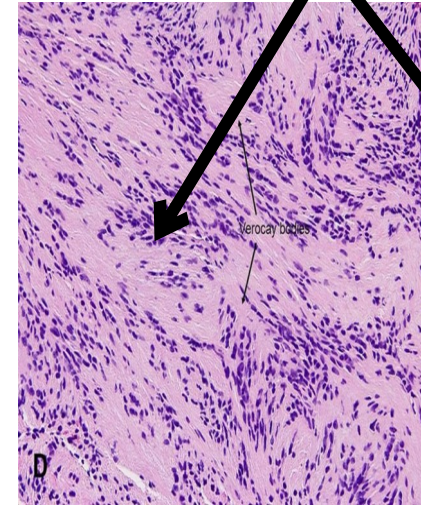


from Schwann cells.

## Comment

1. composed of mixture of two growth patterns:
2. **Antoni A growth pattern** formed of :
  - elongated cells arranged in bundles with
  - nuclear **palisading** (the nuclei are arranged side by side in each bundle)
  - cytoplasmic nuclear free zones are called “**verrocay bodies**”.
3. **Antoni B growth pattern** formed of :
  - less densely cellular elements

### Verrocay bodies





# Glioblastoma multiforme



## Specimen

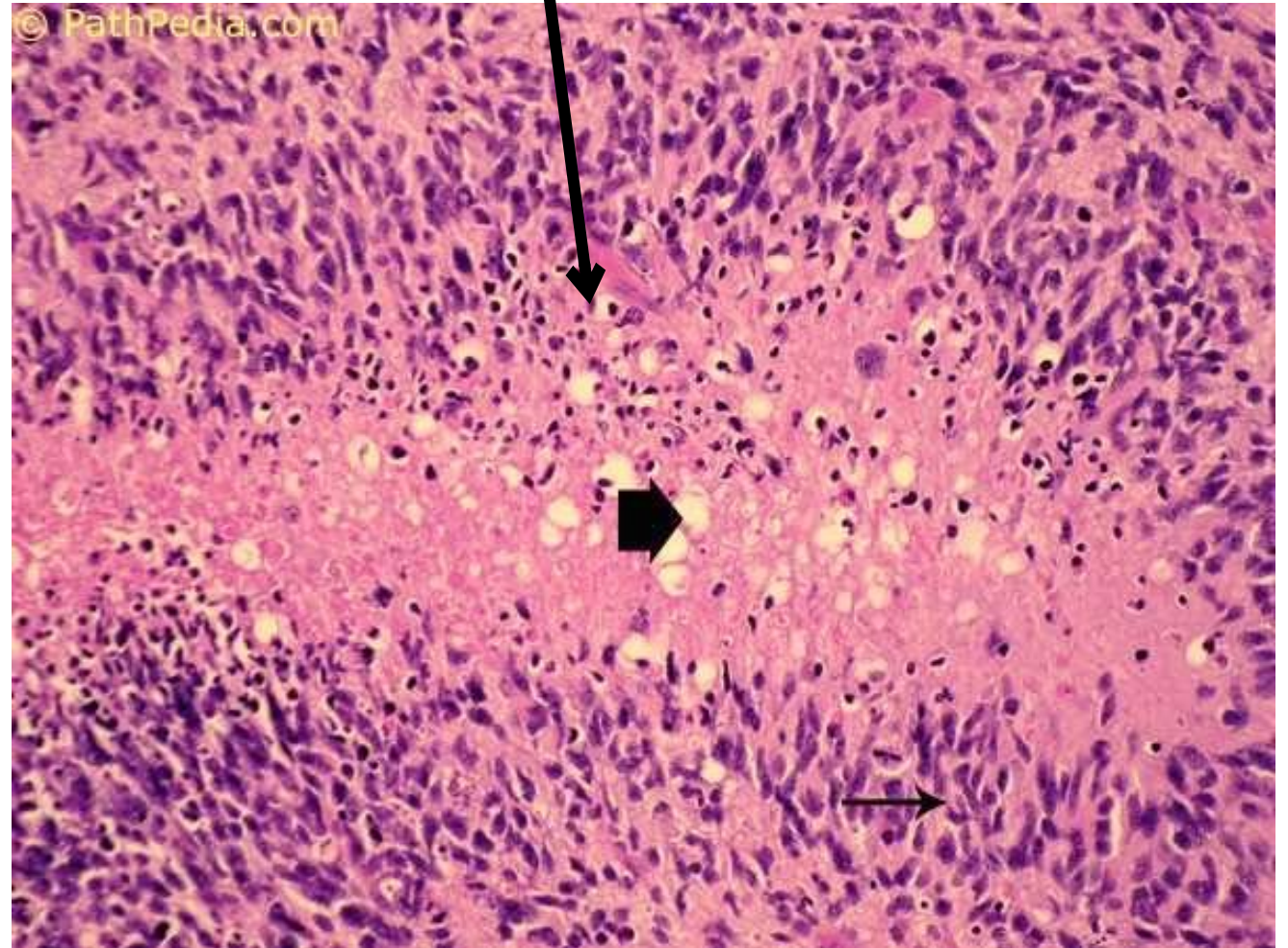
Section in malignant tumor originating from **cerebral cortex**.

## Comment

1. Highly cellular tumor cells
2. **Formed of :**
  - Highly anaplastic cells
  - **Palisading necrosis:** proliferating tumor cells surrounding central area of necrosis

**Diagnosis:** Glioblastoma multiforme

## Palisading Necrosis



[https://www.pathpedia.com/education/eatlas/histopathology/brain\\_and\\_cord/glioblastoma\\_\(gbm\)/glioblastoma-brain-\[2-br006-3\].jpeg?Width=600&Height=450&Format=4](https://www.pathpedia.com/education/eatlas/histopathology/brain_and_cord/glioblastoma_(gbm)/glioblastoma-brain-[2-br006-3].jpeg?Width=600&Height=450&Format=4)



# Quiz



**TEST** Yourself!

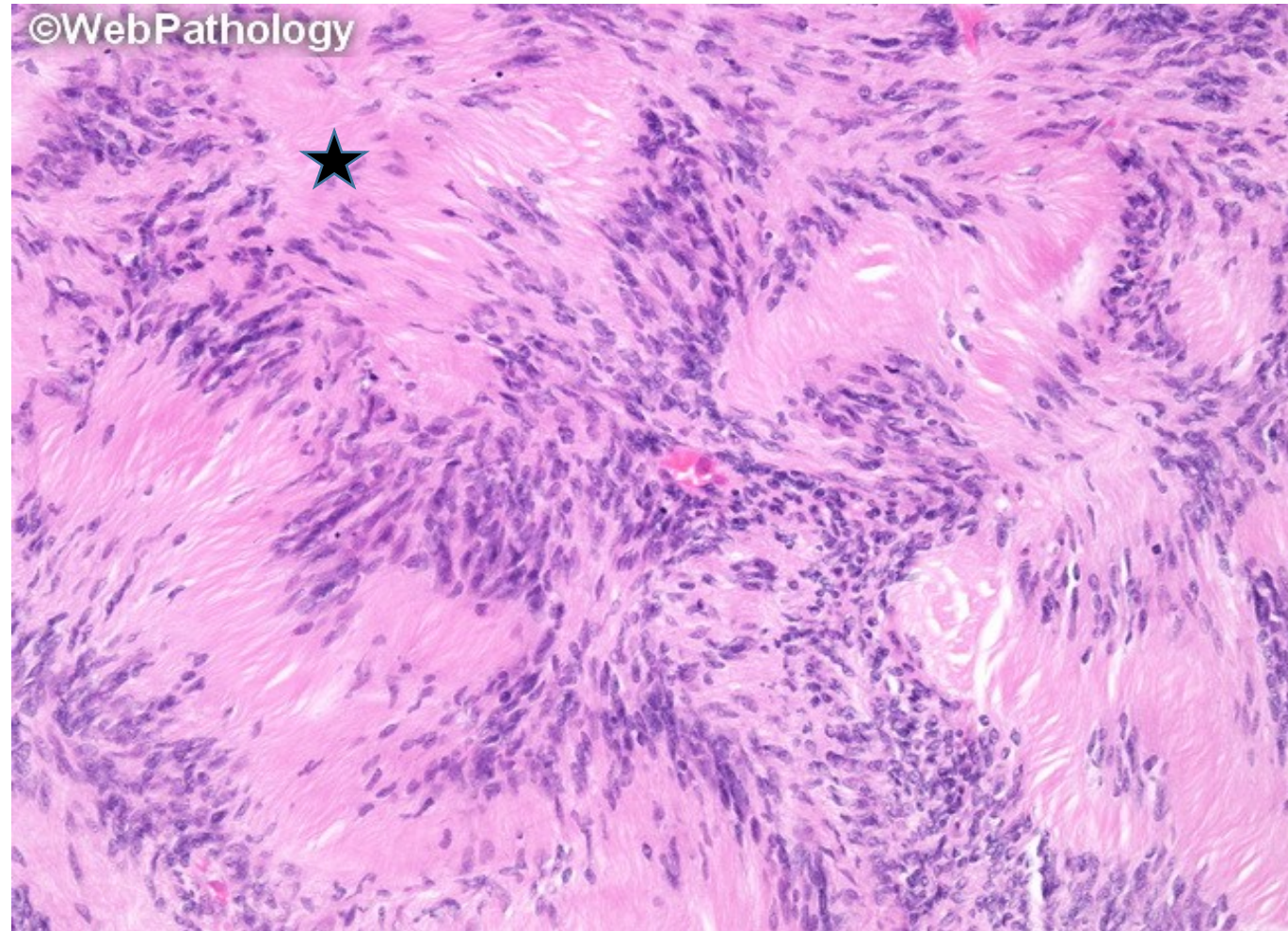




# Quiz



- 1. Identify the lesion**
- 2. Name the growth pattern seen in this lesion**
- 3. Name the structure marked by the star**

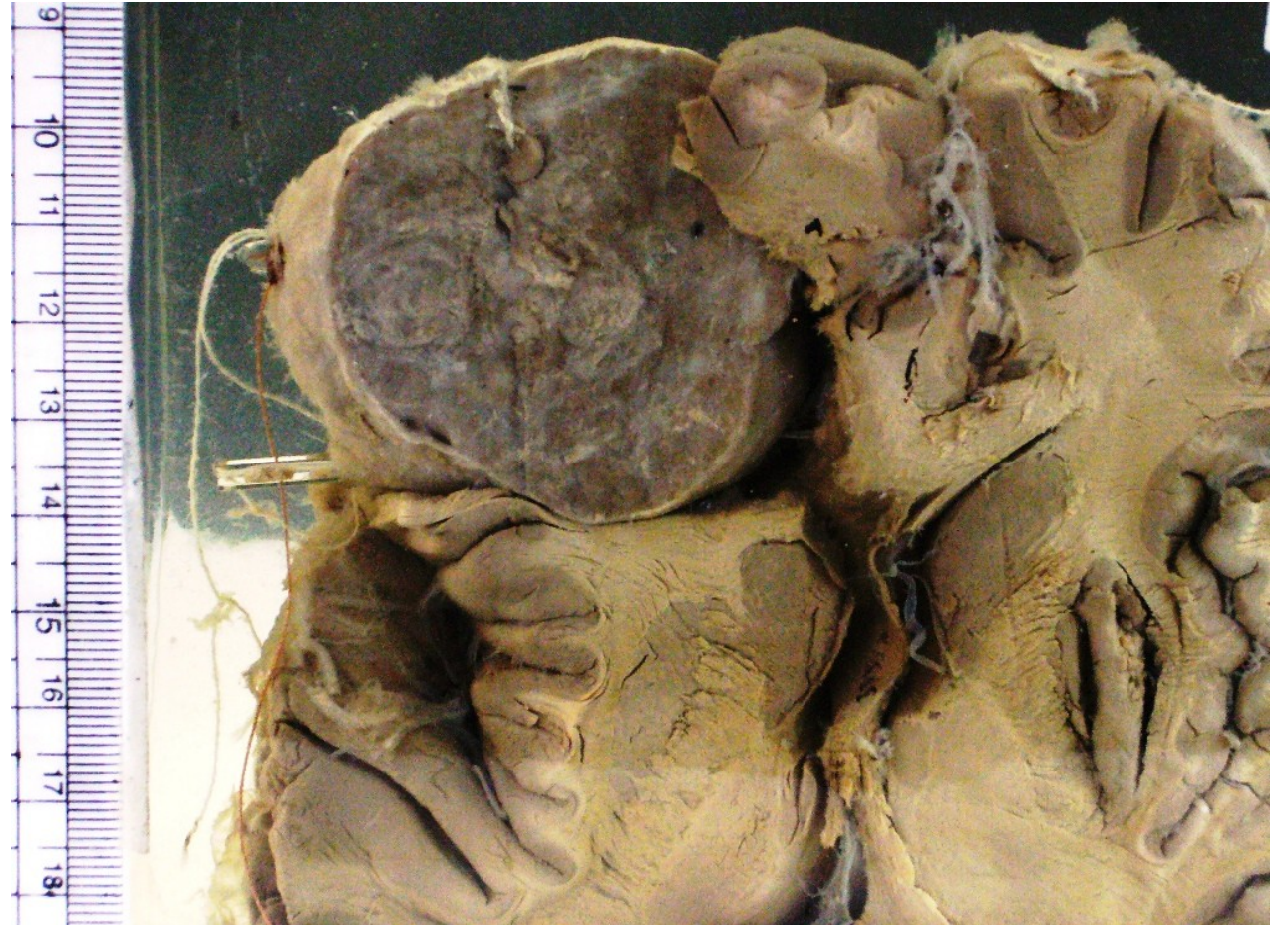




# Quiz



- 1. Identify the lesion**
- 2. Describe it**





## CNS Case



# Case



- ❑ A man 45 years old presented to the emergency room by recurrent attacks of headache not responding to treatment.



<http://reachingutopia.com/wp-content/uploads/2013/05/man-headache.jpg>

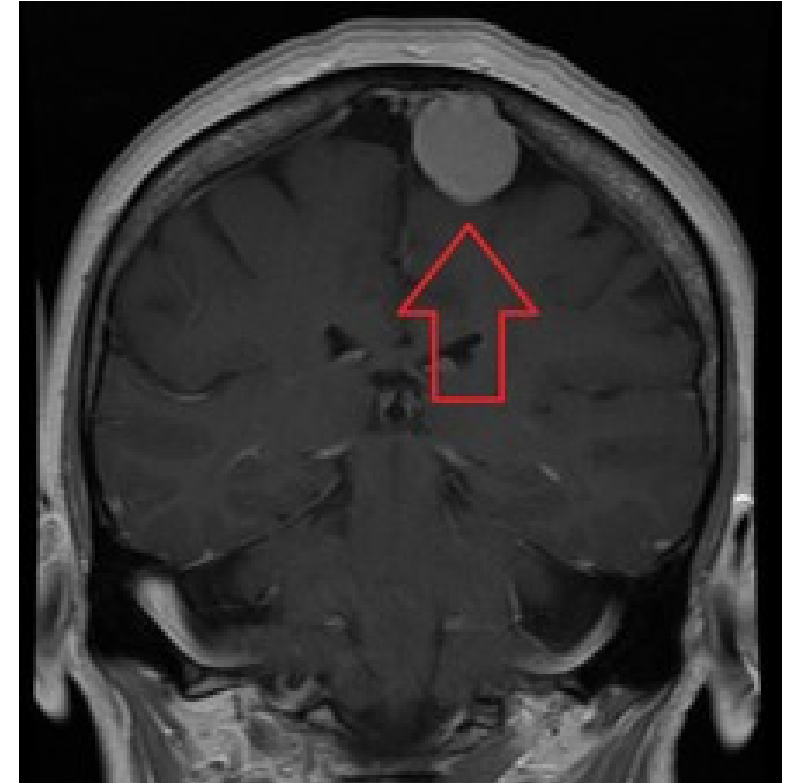




# Case



- ❑ MRI on the brain revealed a dural attached mass



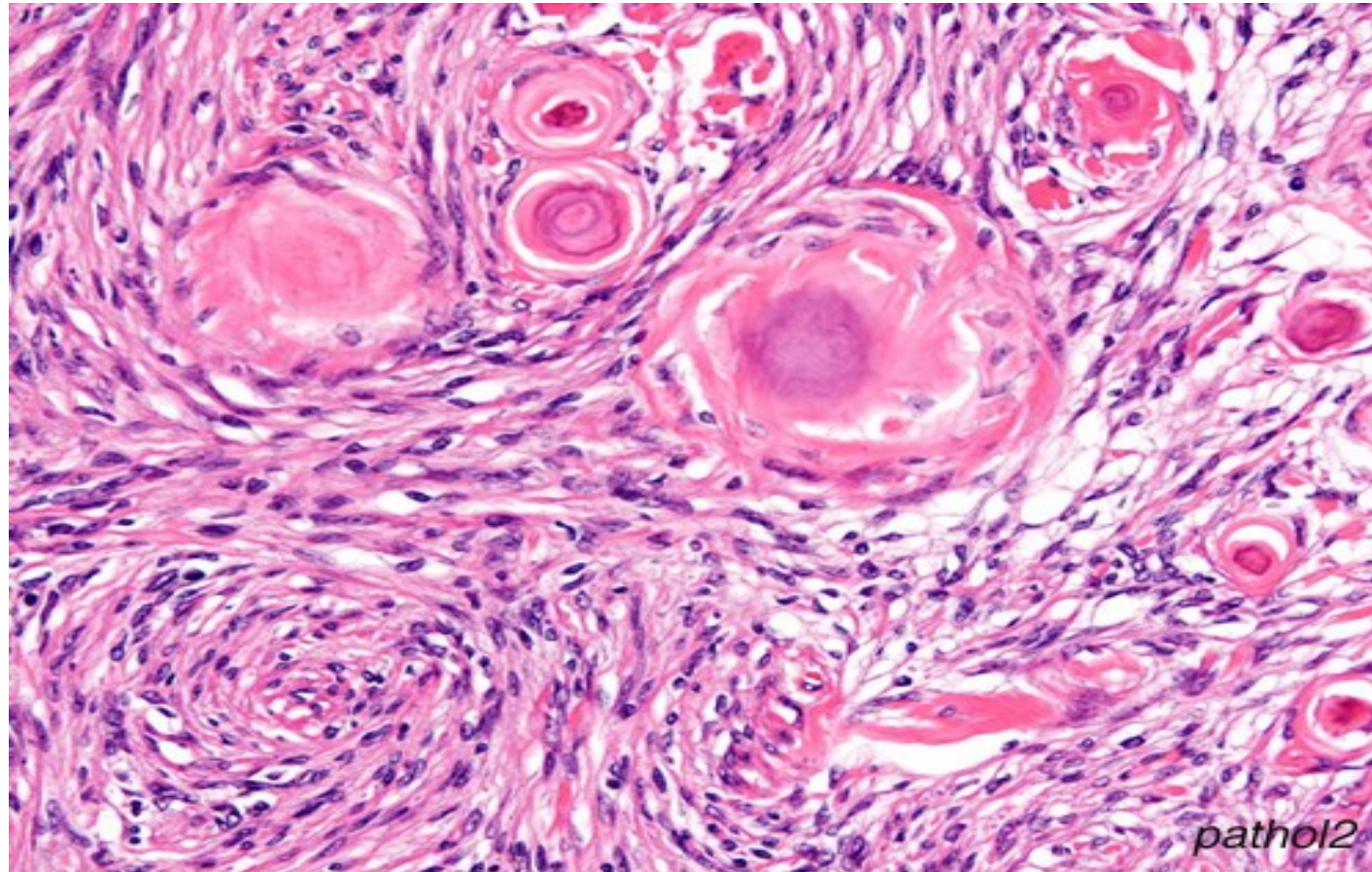
<https://upload.wikimedia.org/wikipedia/commons/thumb/6/68/MRIMeningioma.png/220px-MRIMeningioma.png>



# Case



A biopsy was taken , which revealed the following picture



# Case



- 1) What is your diagnosis?
- 2) What is WHO grade of this lesion?
- 3) From where does it arise?
- 4) Describe the gross and microscopic picture of this lesion.







to all of you  
**big**  
thanks!

